

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1623PAZ

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS	4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/USPAT2
NEWS	5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	9	JAN 30	Saved answer limit increased
NEWS	10	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS	11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	12	FEB 22	Status of current WO (PCT) information on STN
NEWS	13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	17	FEB 28	TOXCENTER reloaded with enhancements
NEWS	18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	19	MAR 01	INSPEC reloaded and enhanced
NEWS	20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS	21	MAR 08	X.25 communication option no longer available after June 2006
NEWS	22	MAR 22	EMBASE is now updated on a daily basis
NEWS EXPRESS			FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <a href="http://download.cas.org/express/v8.0-Discover/">http://download.cas.org/express/v8.0-Discover/</a>
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 07:13:01 ON 03 APR 2006

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 07:13:21 ON 03 APR 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 MAR 2006 HIGHEST RN 878899-57-1

DICTIONARY FILE UPDATES: 31 MAR 2006 HIGHEST RN 878899-57-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

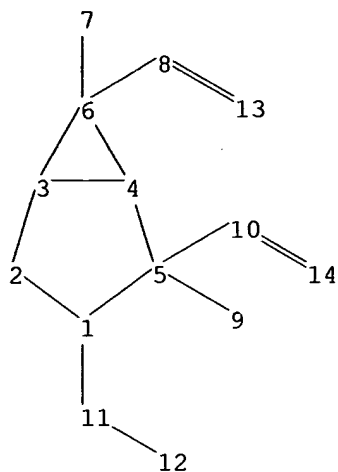
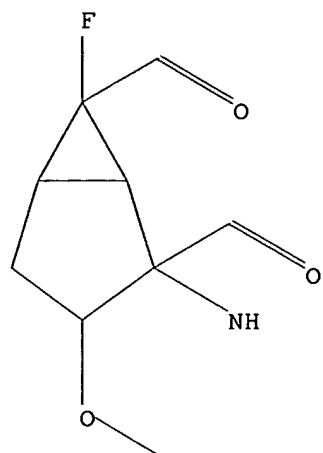
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Documents and Settings\PZucker\My Documents\Examination Auxillary files\10500101\10500101 clm 2 core.str



```

chain nodes :
7 8 9 10 11 12 13 14
ring nodes :
1 2 3 4 5 6
chain bonds :
1-11 5-9 5-10 6-7 6-8 8-13 10-14 11-12
ring bonds :
1-2 1-5 2-3 3-4 3-6 4-5 4-6
exact/norm bonds :
1-2 1-5 1-11 2-3 3-4 3-6 4-5 4-6 5-9 8-13 10-14 11-12
exact bonds :
5-10 6-7 6-8

```

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS

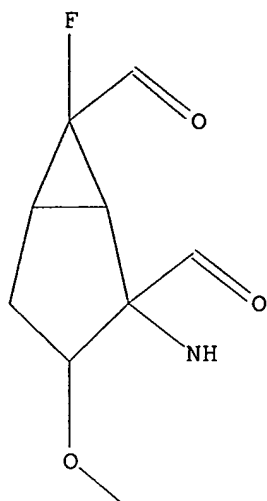
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L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> search l1 sss sam

SAMPLE SEARCH INITIATED 07:13:47 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS

9 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 33 TO 447

PROJECTED ANSWERS: 9 TO 360

L2 9 SEA SSS SAM L1

=> d scan

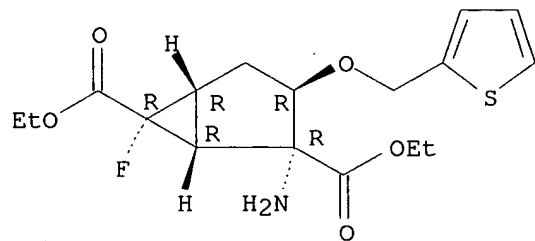
L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-thienylmethoxy)-, diethyl ester, (1R,2R,3R,5R,6R)- (9CI)

MF C17 H22 F N O5 S

CI COM

Absolute stereochemistry. Rotation (+).

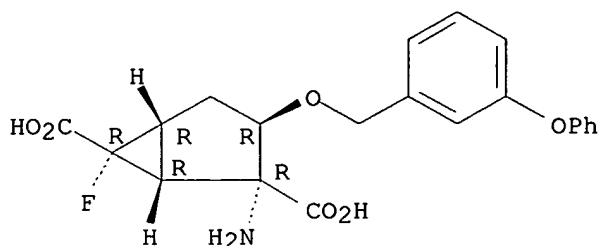


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):9

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI)  
MF C21 H20 F N O6

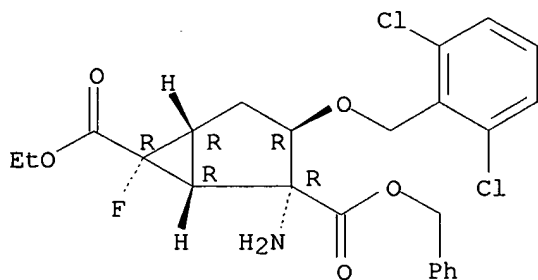
Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)  
MF C24 H24 Cl2 F N O5

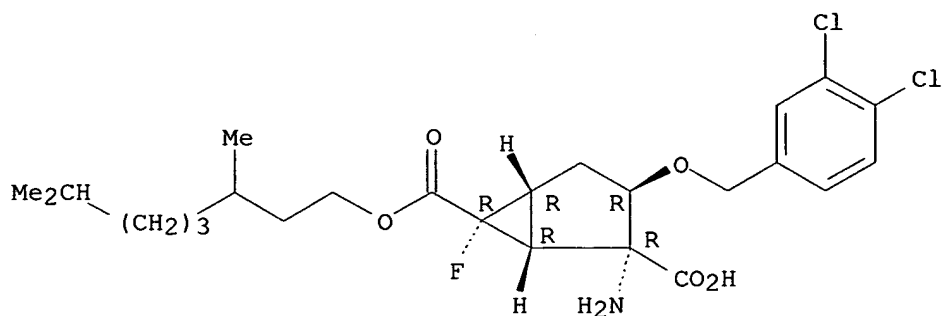
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(3,7-dimethyloctyl) ester, (1R,2R,3R,5R,6R)- (9CI)  
MF C25 H34 Cl2 F N O5

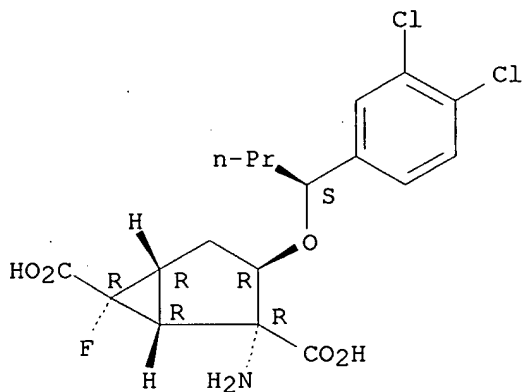
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-(9CI)  
 MF C18 H20 Cl2 F N O5

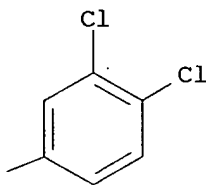
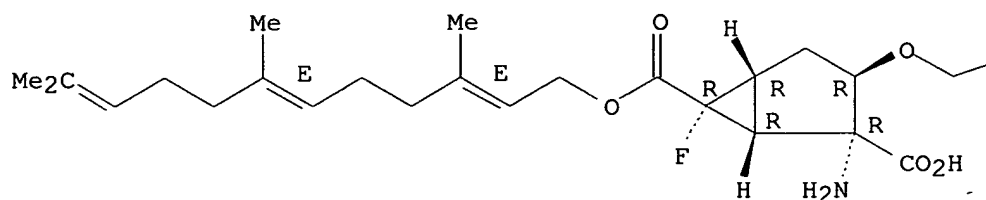
Absolute stereochemistry. Rotation (+).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrienyl] ester, (1R,2R,3R,5R,6R)-(9CI)  
 MF C30 H38 Cl2 F N O5

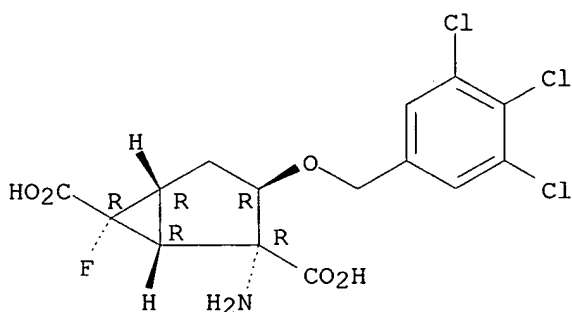
Absolute stereochemistry.  
 Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (9CI)  
 MF C15 H13 Cl3 F N O5

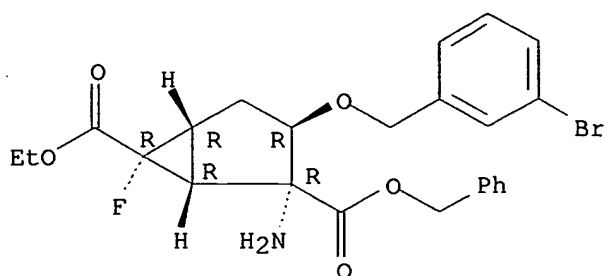
Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)  
 MF C24 H25 Br F N O5  
 CI COM

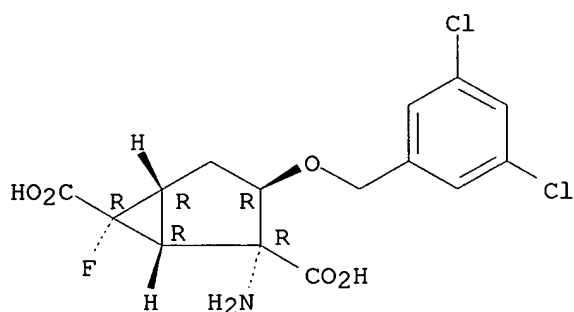
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)  
 MF C15 H14 Cl2 F N O5

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.88	1.09

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 07:14:15 ON 03 APR 2006

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FILE COVERS 1907 - 3 Apr 2006 VOL 144 ISS 15  
FILE LAST UPDATED: 2 Apr 2006 (20060402/ED)

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<http://www.cas.org/infopolicy.html>

=> 12

L3 4 L2

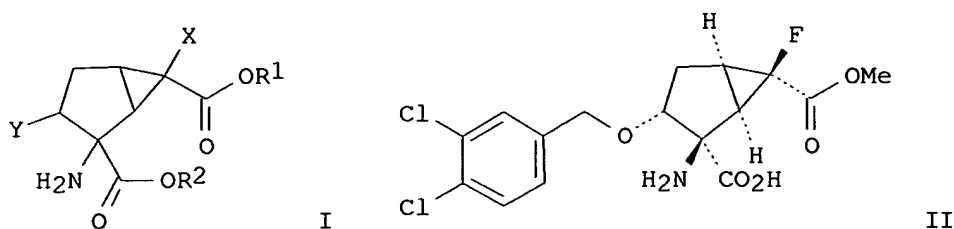
=> d 13 1-4 ti fbib abs

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as  
Group II metabotropic glutamate receptor antagonists  
AN 2005:14355 CAPLUS  
DN 142:113634  
TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as  
Group II metabotropic glutamate receptor antagonists  
IN Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro  
PA Taisho Pharmaceutical Co., Ltd., Japan  
SO PCT Int. Appl., 144 pp.  
CODEN: PIXXD2  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005000791	A1	20050106	WO 2004-JP9398	20040625
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				JP 2003-181930	A 20030626
				JP 2003-373511	A 20031031
				JP 2004-128663	A 20040423
AU	2004252017	A1	20050106	AU 2004-252017	20040625
				JP 2003-181930	A 20030626
				JP 2003-373511	A 20031031
				JP 2004-128663	A 20040423
				WO 2004-JP9398	W 20040625
CA	2530706	AA	20050106	CA 2004-2530706	20040625
				JP 2003-181930	A 20030626
				JP 2003-373511	A 20031031
				JP 2004-128663	A 20040423
				WO 2004-JP9398	W 20040625
EP	1637517	A1	20060322	EP 2004-746867	20040625
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
				JP 2003-181930	A 20030626
				JP 2003-373511	A 20031031
				JP 2004-128663	A 20040423

OS MARPAT 142:113634

GI



AB The title compds. I [wherein R1 and R2 = independently alkyl, alkenyl, alkynyl, etc.; X = H or F; Y = (un)substituted alkoxy, SH, amino, etc.] or hydrates or pharmaceutically acceptable salts thereof are prepared as Group II metabotropic glutamate receptor antagonists. For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic effect on Group II metabotropic glutamate receptor in rat. I are useful for the treatment of schizophrenia, anxiety, and diseases related to these, i.e., psychiatric disorders such as depression, bipolar disorder, and epilepsy (no data).

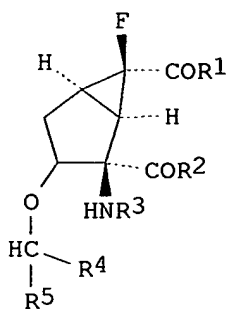
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN  
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases  
AN 2004:1038326 CAPLUS  
DN 142:16843  
TI mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases  
IN Nakazato, Atsuro; Taki, Shigeyuki; Sakagami, Kazunari; Dean, Reiko; Ota, Hiroyuki; Hirota, Shiho; Yasuhara, Akitaka  
PA Taisho Pharmaceutical Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 70 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2004339199	A2	20041202	JP 2004-86153	20040324
				JP 2003-117907	A 20030423

OS MARPAT 142:16843

GI



AB The antidepressant mGlu2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivs., salts, and hydrates are claimed for treatment of nervous system diseases, including bipolar affective disorder, psychiatry disorder, anxiety, epilepsy, drug dependence, cognition disorder, Alzheimer's disease, Huntington's disease, Parkinson disease, muscle stiffness, brain ischemia, spinal cord injury, head injury, etc.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists

AN 2004:620394 CAPLUS

DN 141:243074

TI Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists

AU Nakazato, Atsuro; Sakagami, Kazunari; Yasuhara, Akito; Ohta, Hiroshi; Yoshikawa, Ryoko; Itoh, Manabu; Nakamura, Masato; Chaki, Shigeyuki

CS Medicinal Chemistry Laboratory, Taisho Pharmaceutical Co. Ltd., Kita-ku, Saitama-shi, Saitama, 331-9530, Japan

SO Journal of Medicinal Chemistry (2004), 47(18), 4570-4587

CODEN: JMCMAR; ISSN: 0022-2623

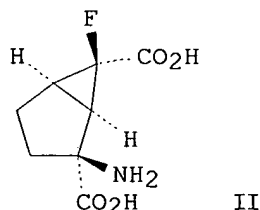
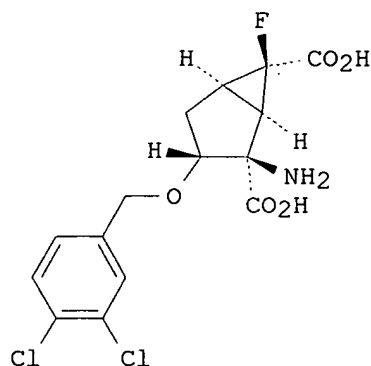
PB American Chemical Society

DT Journal

LA English

OS CASREACT 141:243074

GI



AB Group II metabotropic glutamate receptor (mGluR) antagonists,

3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., e.g., I, were discovered by the incorporation of a hydroxy or alkoxyl group onto the C-3 portion of selective and potent group II mGluR agonist II. Among these compds., I (MGS0039) was a highly selective and potent group II mGluR antagonist with the best pharmacokinetic profile. I exhibited high affinities for mGlu 2 ( $K_i = 2.38 \pm 0.40$  nM) and mGlu 3 ( $4.46 \pm 0.31$  nM) but low affinity for mGluR 7 ( $K_i = 664 \pm 106$  nM), and potent antagonist activities for mGlu 2 ( $IC_{50} = 20.0 \pm 3.67$  nM) and mGluR 3 ( $IC_{50} = 24.0 \pm 3.54$  nM) but much less potent antagonist activities for mGlu 4 ( $IC_{50} = 1740 \pm 1080$  nM), mGlu 6 ( $IC_{50} = 2060 \pm 1270$  nM), mGlu 1 ( $IC_{50} = 93300 \pm 14600$  nM), and mGluR 5 ( $IC_{50} = 117000 \pm 38600$  nM). No significant agonist activities of I were found for mGluRs 2, 3, 4, 6, 1, and 5 ( $EC_{50} > 100000$  nM). Furthermore, I exhibited dose-dependent oral absorption (plasma  $C_{max}$ :  $214 \pm 56.7$ ,  $932 \pm 235$ , and  $2960 \pm 1150$  ng/mL for 3 mg/kg, 10 mg/kg, and 30 mg/kg, po, resp.) and acceptable blood-brain barrier penetration (brain  $C_{max}$ : 13.2 ng/mL for 10 mg/kg, po 6 h). The synthesis, in vitro pharmacol. profile, and structure-activity relationships of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., and pharmacokinetic profiles of several typical compds, are presented.

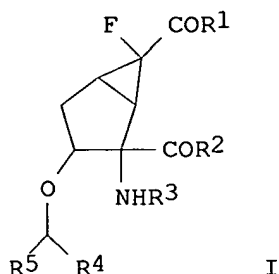
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN  
TI 6-Fluorobicyclo[3.1.0]hexane derivatives  
AN 2003:591035 CAPLUS  
DN 139:143973  
TI 6-Fluorobicyclo[3.1.0]hexane derivatives  
IN Nakazato, Atsuro; Chaki, Shigeyuki; Sakagami, Kazunari; Dean, Ryoko; Ohta, Hiroshi; Hirota, Shiho; Yasuhara, Akito  
PA Taisho Pharmaceutical Co.,ltd., Japan  
SO PCT Int. Appl., 98 pp.  
CODEN: PIXXD2  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003061698	A1	20030731	WO 2002-JP13693	20021226
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				JP 2001-395797	A 20011227
	CA 2471642	AA	20030731	CA 2002-2471642	20021226
				JP 2001-395797	A 20011227
				WO 2002-JP13693	W 20021226
	EP 1459765	A1	20040922	EP 2002-793421	20021226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
				JP 2001-395797	A 20011227
				WO 2002-JP13693	W 20021226
	BR 2002015462	A	20041130	BR 2002-15462	20021226
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US 2005119345	A1	20050602	US 2003-500101	20021226
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ZA 2005002085	A	20050629	ZA 2005-2085	20021226
			JP 2001-395797	A 20011227
ZA 2004004795	A	20050617	ZA 2004-4795	20040617
			JP 2001-395797	A 20011227

OS MARPAT 139:143973  
GI



AB Antidepressants containing as the active ingredient compds. having group II metabotropic glutamate receptor antagonism; and 2-amino-3-alkoxy-6-fluorobicyclo[3.1.0]-hexane-2,6-dicarboxylic acid derivs. represented by the general formula [I], pharmaceutically acceptable salts thereof, or hydrates of the salts: I wherein R1 and R2 may be the same or different from each other and are each hydroxyl, C1-10 alkoxy, or the like; R3 is C1-10 acyl, C1-6 alkoxy-C1-6 acyl, or the like; and R4 and R5 may be the same or different from each other and are each hydrogen, C1-10 alkyl, or the like.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> search l1 sss samfile reg

**REGISTRY INITIATED**

Substance data SEARCH and crossover from CAS REGISTRY in progress...  
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 07:19:40 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 12 TO ITERATE

100.0% PROCESSED 12 ITERATIONS 9 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 33 TO 447  
PROJECTED ANSWERS: 9 TO 360

L4 9 SEA SSS SAM L1

L5

4 L4

MISSING OPERATOR L5 SSS

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.46	17.09
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.00

FILE 'REGISTRY' ENTERED AT 07:19:51 ON 03 APR 2006  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 MAR 2006 HIGHEST RN 878899-57-1  
DICTIONARY FILE UPDATES: 31 MAR 2006 HIGHEST RN 878899-57-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> search l1 full

ENTER TYPE OF SEARCH (SSS), CSS, FAMILY, OR EXACT:sss  
FULL SEARCH INITIATED 07:20:25 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 280 TO ITERATE

100.0% PROCESSED 280 ITERATIONS 224 ANSWERS  
SEARCH TIME: 00.00.01

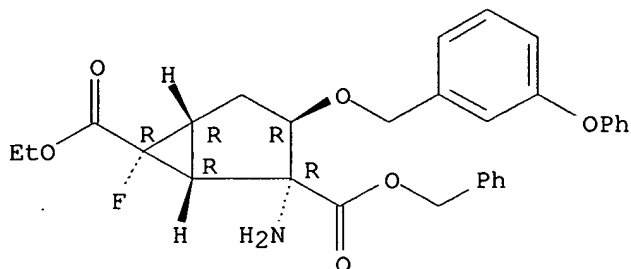
L6

224 SEA SSS FUL L1

=> d scan

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)-(9CI)  
MF C30 H30 F N O6  
CI COM

Absolute stereochemistry.

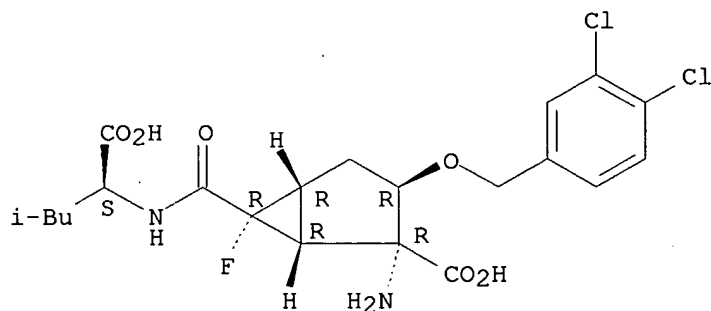


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):20

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN Bicyclo[3.1.0]hexane-2-carboxylic acid, 2-amino-6-[[[(1S)-1-carboxy-3-methylbutyl]amino]carbonyl]-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-(9CI)  
MF C21 H25 Cl2 F N2 O6

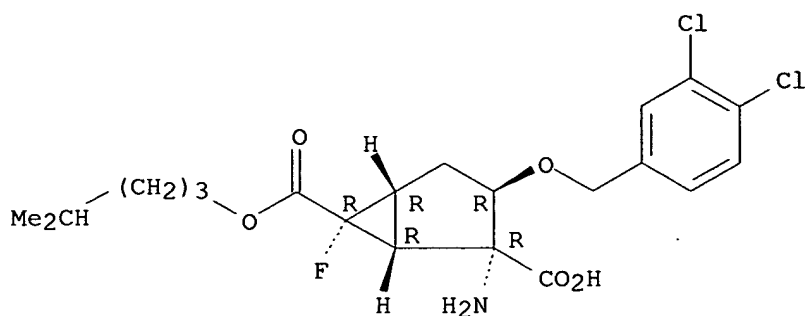
Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(4-methylpentyl) ester, (1R,2R,3R,5R,6R)-(9CI)  
MF C21 H26 Cl2 F N O5

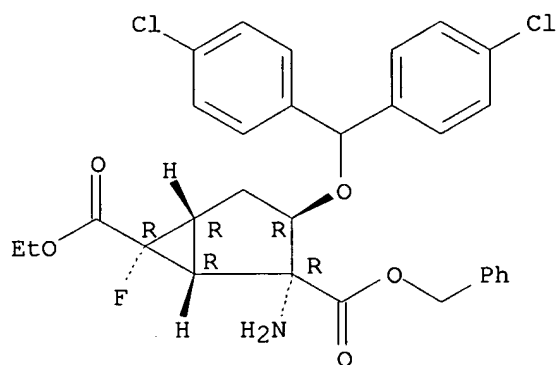
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)  
 MF C30 H28 Cl2 F N O5  
 CI COM

Absolute stereochemistry.

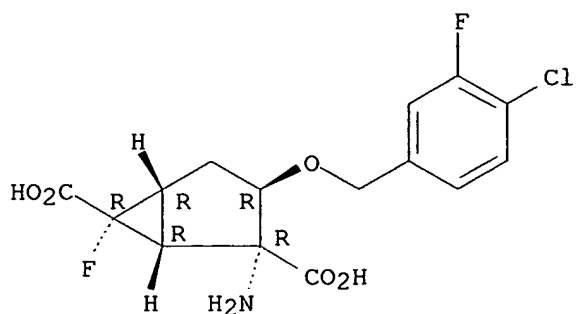


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chloro-3-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)  
 MF C15 H14 Cl F2 N O5

Absolute stereochemistry. Rotation (-).

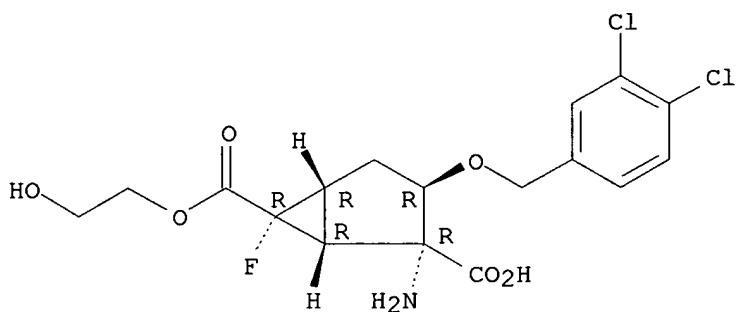




\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
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 MF C17 H18 Cl2 F N O6

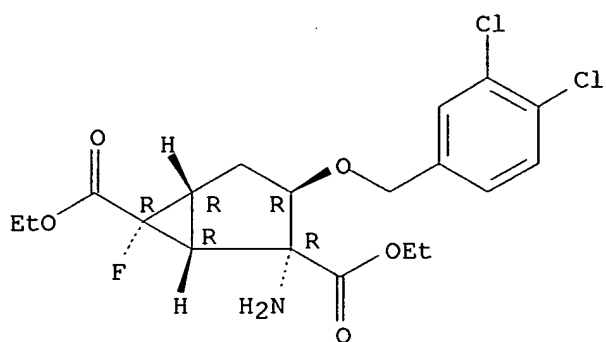
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, diethyl ester, monosodium salt, (1R,2R,3R,5R,6R)- (9CI)  
 MF C19 H22 Cl2 F N O5 . Na

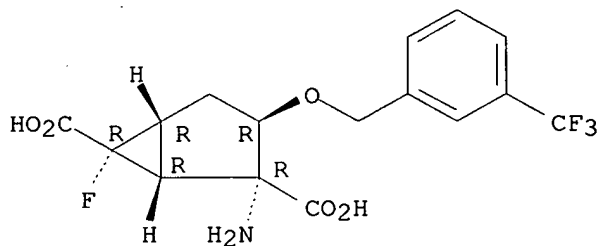
Absolute stereochemistry. Rotation (+).



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[3-(trifluoromethyl)phenyl]methoxy]-, (1R,2R,3R,5R,6R)- (9CI)  
 MF C16 H15 F4 N O5

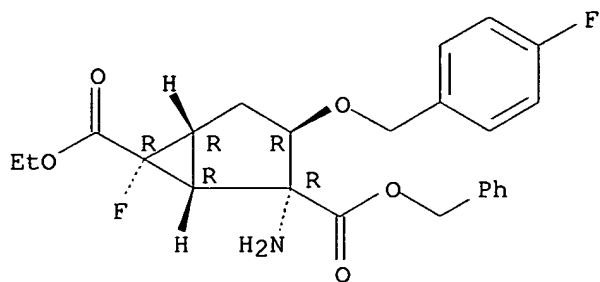
Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(4-fluorophenyl)methoxy]-, 6-ethyl 2-(phenylmethyl) ester, (1R,2R,3R,5R,6R)- (9CI)  
 MF C24 H25 F2 N O5  
 CI COM

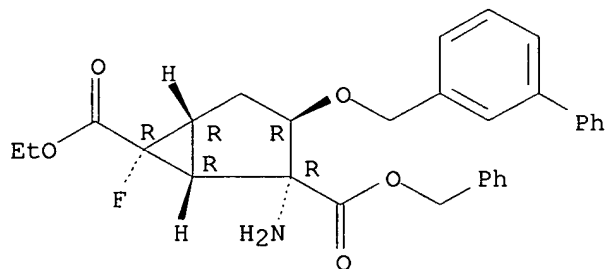
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
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 MF C30 H30 F N O5 . Na

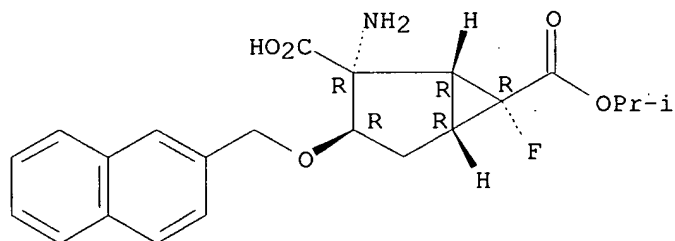
Absolute stereochemistry.



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-naphthalenylmethoxy)-, 6-(1-methylethyl) ester, (1R,2R,3R,5R,6R)- (9CI)  
 MF C22 H24 F N O5

Absolute stereochemistry.



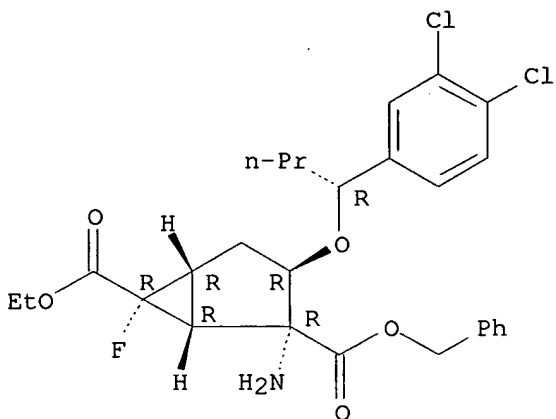
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L6 224 ANSWERS   REGISTRY   COPYRIGHT 2006 ACS on STN
IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1R)-1-(3,4-
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   (1R,2R,3R,5R,6R)- (9CI)
MF C27 H30 Cl2 F N O5
CI COM

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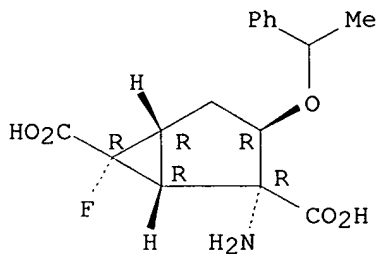
Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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MF C16 H18 F N O5

Absolute stereochemistry.

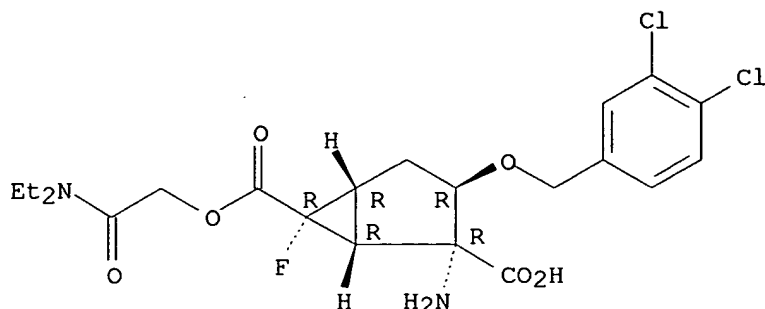


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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dichlorophenyl)methoxy]-6-fluoro-, 6-[2-(diethylamino)-2-oxoethyl] ester,  
 (1R,2R,3R,5R,6R)- (9CI)  
 MF C21 H25 Cl2 F N2 O6

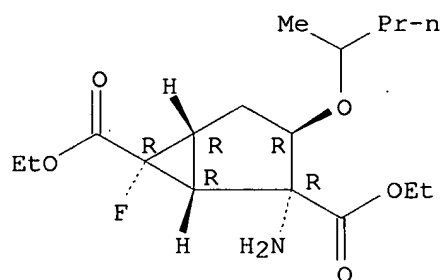
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
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 MF C17 H28 F N O5 . Na

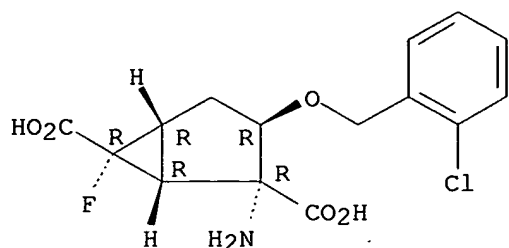
Absolute stereochemistry.



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)  
 MF C15 H15 Cl F N O5

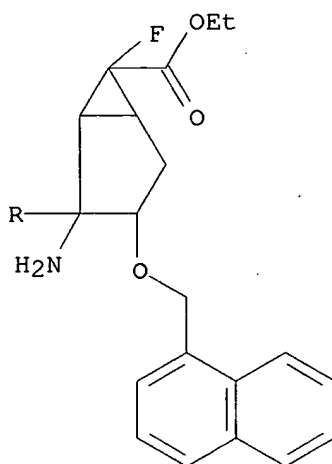
Absolute stereochemistry. Rotation (-).



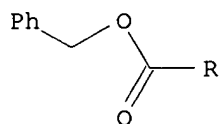
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
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 MF C28 H28 F N O5  
 CI COM

PAGE 1-A

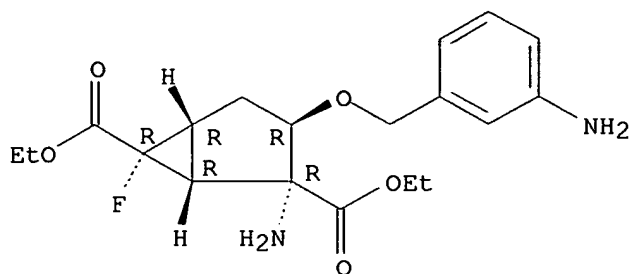


PAGE 2-A



L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-aminophenyl)methoxy]-6-fluoro-, diethyl ester, monosodium salt, (1R,2R,3R,5R,6R)-(9CI)  
 MF C19 H25 F N2 O5 . Na

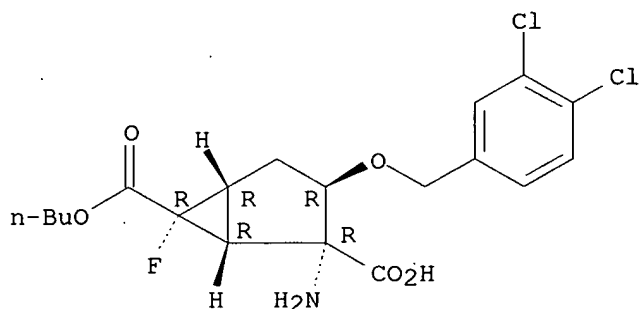
Absolute stereochemistry. Rotation (-).



● Na

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
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 MF C19 H22 Cl2 F N O5  
 CI COM

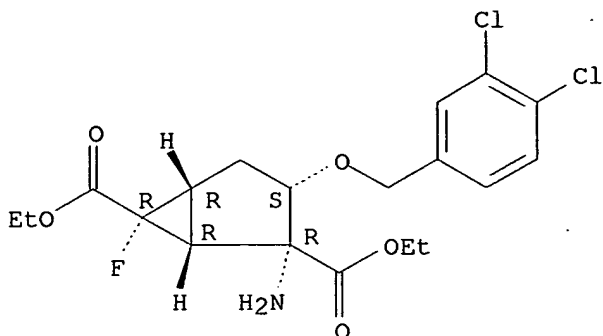
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
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 MF C19 H22 Cl2 F N O5

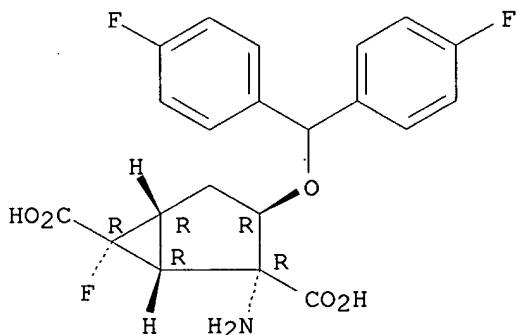
Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L6 224 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
 IN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (9CI)  
 MF C21 H18 F3 N O5

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

167.38

184.47

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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FILE 'CAPLUS' ENTERED AT 07:21:12 ON 03 APR 2006

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FILE LAST UPDATED: 2 Apr 2006 (20060402/ED)

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=> 16

L7 11 L6

=> d his

(FILE 'HOME' ENTERED AT 07:13:01 ON 03 APR 2006)

FILE 'REGISTRY' ENTERED AT 07:13:21 ON 03 APR 2006

L1 STRUCTURE UPLOADED

L2 9 SEARCH L1 SSS SAM

FILE 'CAPLUS' ENTERED AT 07:14:15 ON 03 APR 2006

L3 4 L2

S L1 SSS SAMFILE REG

FILE 'REGISTRY' ENTERED AT 07:19:40 ON 03 APR 2006

L4 9 S L1

FILE 'CAPLUS' ENTERED AT 07:19:40 ON 03 APR 2006

L5 4 S L4

FILE 'REGISTRY' ENTERED AT 07:19:51 ON 03 APR 2006

L6 224 SEARCH L1 FULL SSS

FILE 'CAPLUS' ENTERED AT 07:21:12 ON 03 APR 2006

L7 11 L6

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L8 7 L7 NOT L5

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L8 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

TI A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases extracellular dopamine levels in the nucleus accumbens shell

AN 2005:1351480 CAPLUS

DN 144:81056

TI A metabotropic glutamate 2/3 receptor antagonist, MGS0039, increases extracellular dopamine levels in the nucleus accumbens shell

AU Karasawa, Jun-ichi; Yoshimizu, Takao; Chaki, Shigeyuki

CS Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan

SO Neuroscience Letters (2006), 393(2-3), 127-130

CODEN: NELED5; ISSN: 0304-3940

PB Elsevier Ltd.

DT Journal  
LA English  
AB MGS0039, a potent and selective metabotropic glutamate 2/3 (mGlu 2/3) receptor antagonist, exhibits antidepressant-like activities in some animal models. In the present study, the authors examined the effect of MGS0039 on extracellular dopamine levels in the rat nucleus accumbens (NAc) shell using in vivo microdialysis evaluation because accumbal dopamine has been implicated in depression. Local application of MGS0039 into the NAc shell at 10  $\mu$ M significantly increased extracellular dopamine levels in the NAc shell in freely moving rats. In contrast, local application of 10  $\mu$ M of LY354740, an mGlu 2/3 receptor agonist, significantly decreased extracellular dopamine levels in the same brain region. These findings suggest that dopamine release in the NAc shell is regulated by mGlu 2/3 receptors, and that the effect on dopamine levels in the NAc shell may partially explain the antidepressant-like properties of mGlu 2/3 receptor antagonists.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist  
AN 2005:298938 CAPLUS  
DN 142:423678  
TI AMPA receptor stimulation mediates the antidepressant-like effect of a group II metabotropic glutamate receptor antagonist  
AU Karasawa, Jun-Ichi; Shimazaki, Toshiharu; Kawashima, Naoya; Chaki, Shigeyuki  
CS Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan  
SO Brain Research (2005), 1042(1), 92-98  
CODEN: BRREAP; ISSN: 0006-8993  
PB Elsevier B.V.  
DT Journal  
LA English  
AB (1R,2R,3R,5R,6R)-2-Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a selective group II metabotropic glutamate receptor (mGluR) antagonist, exhibits antidepressant-like activities in rodent models. In the present studies, to clarify the involvement of  $\alpha$ -amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) receptor activation in exhibition of the antidepressant-like properties of MGS0039, the authors examined the effect of an AMPA receptor antagonist, 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(f)quinoxaline (NBQX), on the antidepressant-like effect of MGS0039 in the mouse tail suspension test. The authors also examined the effects of NBQX on increased serotonin release after treatment with MGS0039 in the rat medial prefrontal cortex (mPFC) using in vivo microdialysis evaluation. In the tail suspension test, MGS0039 (0.3-3 mg/kg, i.p.) treatment dose-dependently and significantly reduced immobility time. Pretreatment with NBQX (10 mg/kg, s.c.) significantly prevented the antidepressant-like effect of MGS0039 in the tail suspension test, while NBQX itself had no effect on immobility time. In the microdialysis evaluation, administration of MGS0039 (10 mg/kg, i.p.) significantly increased serotonin levels in mPFC in freely moving rats, while NBQX (1 mg/kg, i.p.) itself had no effect on serotonin release in this region. Pretreatment with NBQX significantly attenuated the increase in serotonin release by MGS0039. These findings suggest that stimulation of postsynaptic AMPA receptors plays a role in mediating the pharmacol. effects of MGS0039.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors

AN 2005:234178 CAPLUS

DN 142:367493

TI Neuropharmacological profiles of antagonists of group II metabotropic glutamate receptors

AU Kawashima, Naoya; Karasawa, Jun-ichi; Shimazaki, Toshiharu; Chaki, Shigeyuki; Okuyama, Shigeru; Yasuhara, Akito; Nakazato, Atsuro

CS Research Strategy Group, Pharmaceutical Business Division, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan

SO Neuroscience Letters (2005), 378(3), 131-134

CODEN: NELED5; ISSN: 0304-3940

PB Elsevier Ltd.

DT Journal

LA English

AB Glutamatergic abnormalities play roles in several psychiatric disorders. Glutamate acts at two classes of receptors, ionotropic and metabotropic glutamate receptors (mGluR), the latter is classified into three group, based on receptor homol. and signaling mechanisms. Among them, recent pharmacol. and histochem. studies suggest that the group II mGluR (mGluR2 and mGluR3) plays crucial roles in the control of emotional states. We previously reported that MGS0039, a selective group II mGluR antagonist, exhibited dose-dependent antidepressant-like effects in some animal models. However, the mechanism by which group II mGluR antagonists exhibit such effects is still unclear. In the present two studies, we examined neuropharmacol. effects of group II mGluR antagonists on monoaminergic neurons. In an electrophysiol. study, MGS0039 dose-dependently and significantly increased the firing rate of dorsal raphe nucleus (DRN) serotonergic neurons. LY341495, another group II mGluR antagonist, also increased DRN serotonergic neural activity significantly. Consistent with the findings of this electrophysiol. study, MGS0039 significantly increased extracellular level of serotonin in rat medial prefrontal cortex in a microdialysis study. In contrast, MGS0039 had no effect on the activity of locus coeruleus noradrenergic neurons. These findings suggest that modulation of serotonergic neuron might be, at least in part, responsible for the antidepressant-like effects of group II mGluR antagonists.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor

AN 2005:14354 CAPLUS

DN 142:113754

TI Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as antagonists of group II metabotropic glutamate receptor

IN Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro

PA Taisho Pharmaceutical Co., Ltd., Japan

SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2005000790	A1	20050106	WO 2004-JP9384	20040625
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

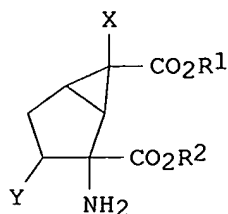
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 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
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 SN, TD, TG

JP 2003-181931

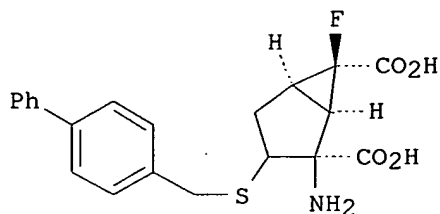
A 20030626

OS MARPAT 142:113754

GI



I



II

AB The title compds. [I; R1, R2 = H, C1-10 alkyl, Ph, naphthyl, mono- or diphenyl-C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, hydroxy-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl, amino-C2-10 alkyl, C1-10 alkoxy-C1-10 alkyl; X = H, F; Y = NH2, SR3, S(O)nR7, SCHR3R4, S(O)nCHR3R4, NHCHR3R4, N(CHR3R4)(CHR5R6), NHCOR3, O2CR7; wherein R3-R6 = H, C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; R7 = C1-10 alkyl, (un)substituted Ph, naphthyl, 1-7 halogen(s)-substituted naphthyl, heteroaryl; n = 1,2], pharmaceutically acceptable salts thereof, or hydrates of either are prepared. These compds., e.g. (II), had an antagonistic effect on a Group II metabotropic glutamate receptor with IC50 of ≤200 nM, and are effective in treatments for and prevention of psychiatric disorders and neurol. diseases.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test

AN 2004:814656 CAPLUS

DN 141:325597

TI Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test

AU Shimazaki, Toshiharu; Iijima, Michihiko; Chaki, Shigeyuki

CS Psychiatric Diseases and Pain Research, Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan

SO European Journal of Pharmacology (2004), 501(1-3), 121-125  
 CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier B.V.

DT Journal

LA English

AB Glutamatergic abnormalities are involved in several psychiatric disorders. Clin. evidence demonstrates altered glutamatergic neurotransmission in patients suffering from obsessive-compulsive disorder. MGS0039, (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzoyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, is a novel group II metabotropic glutamate (mGlu) receptor antagonist. We examined MGS0039's potential anti-obsessive-compulsive disorder activity, using the marble-burying behavior test as a model of obsessive-compulsive disorder. MGS0039 as well as LY341495 ((2S,1'S,2'S)-2-(9-xanthylmethyl)-2-(2'-carboxycyclopropyl)glycine), another group II mGlu receptor antagonist, inhibited marble-burying behavior. We also demonstrated that this effect

was significantly attenuated by a group II mGlu receptor agonist. This data indicates that group II mGlu receptor antagonists may exert anti-obsessive-compulsive disorder effects in clin. use.

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity  
AN 2004:126085 CAPLUS  
DN 141:82129  
TI MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity  
AU Chaki, Shigeyuki; Yoshikawa, Ryoko; Hirota, Shiho; Shimazaki, Toshiharu; Maeda, Maoko; Kawashima, Naoya; Yoshimizu, Takao; Yasuhara, Akito; Sakagami, Kazunari; Okuyama, Shigeru; Nakanishi, Shigetada; Nakazato, Atsuro  
CS Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan  
SO Neuropharmacology (2004), 46(4), 457-467  
CODEN: NEPHBW; ISSN: 0028-3908  
PB Elsevier Science B.V.  
DT Journal  
LA English  
AB The present study describes the pharmacol. profile of (1R,2R,3R,5R,6R)-2-Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a novel group II mGluR antagonist. MGS0039 showed high affinity for both mGluR2 ( $K_i = 2.2$  nM) and mGluR3 ( $K_i = 4.5$  nM), which are comparable to LY341495, another group II mGluR antagonist. MGS0039 attenuated both glutamate-induced inhibition of forskolin-evoked cAMP formation in CHO cells expressing mGluR2 ( $IC_{50} = 20$  nM) or mGluR3 ( $IC_{50} = 24$  nM) and glutamate-increased [ $^{35}$ S]GTP $\gamma$ S binding to mGluR2 ( $pA_{2} = 8.2$ ), which means that MGS0039 acts as an antagonist. MGS0039 shifted the dose-response curve of glutamate-increased [ $^{35}$ S]GTP $\gamma$ S binding rightward without altering the maximal response, and thereby indicating competitive antagonism. MGS0039 showed no significant effects on other mGluRs as well as the other receptors and transporters we studied. MGS0039 (0.3-3 mg/kg, i.p.) as well as LY341495 (0.1-3 mg/kg, i.p.) had dose-dependent antidepressant-like effects in the rat forced swim test and in the mouse tail suspension test. In contrast, MGS0039 (0.3-3 mg/kg, i.p.) had no apparent effect in the rat social interaction test and in the rat elevated plus-maze. These results indicate that MGS0039 is a potent and selective antagonist of group II mGluR, and that group II mGluR antagonists, like MGS0039, have an antidepressant-like potential in exptl. animal models.

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039  
AN 2004:96754 CAPLUS  
DN 140:368470  
TI Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039  
AU Yoshimizu, Takao; Chaki, Shigeyuki  
CS Medicinal Research Laboratories, Medicinal Pharmacology Laboratory, Psychiatric Diseases and Pain Research, Taisho Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan  
SO Biochemical and Biophysical Research Communications (2004), 315(2), 493-496

CODEN: BBRC9; ISSN: 0006-291X

PB Elsevier Science

DT Journal

LA English

AB We have previously reported that MGS0039, a novel antagonist of group II metabotropic glutamate receptors (mGluRs), exerts antidepressant-like effects in exptl. animal models. Recent studies suggest that the behavioral effects of chronic antidepressant treatment are mediated by the stimulation of neurogenesis in the hippocampus. In the present study, we examined the effects of MGS0039 on cell proliferation in the adult mouse hippocampus. MGS0039 (5 or 10 mg/kg) or fluvoxamine was administered chronically to male ICR mice over a period of 14 days. Multiple bromodeoxyuridine (BrdU) administrations were performed after the last drug injection to label dividing cells. Immunohistochem. analyses after BrdU injections revealed that chronic MGS0039 treatment enhanced BrdU-pos. cells in the dentate gyrus (.apprx.62% increase) in the same manner as chronic fluvoxamine treatment. This is the first in vivo study to demonstrate an increase in cell proliferation following a blockade of group II mGluRs. These findings raise the possibility that MGS0039 may exert antidepressant-like effects by modulating cell proliferation in the hippocampus.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
21.02	205.49

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-5.25	-8.25

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NEWS	4 DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/USPAT2
NEWS	5 JAN 13	IPC.8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	6 JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	7 JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	8 JAN 17	IPC 8 in the WPI family of databases including WPIFV

NEWS 9 JAN 30 Saved answer limit increased  
 NEWS 10 JAN 31 Monthly current-awareness alert (SDI) frequency  
 added to TULSA  
 NEWS 11 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist  
 visualization results  
 NEWS 12 FEB 22 Status of current WO (PCT) information on STN  
 NEWS 13 FEB 22 The IPC thesaurus added to additional patent databases on STN  
 NEWS 14 FEB 22 Updates in EPFULL; IPC 8 enhancements added  
 NEWS 15 FEB 27 New STN AnaVist pricing effective March 1, 2006  
 NEWS 16 FEB 28 MEDLINE/LMEDLINE reload improves functionality  
 NEWS 17 FEB 28 TOXCENTER reloaded with enhancements  
 NEWS 18 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral  
 property data  
 NEWS 19 MAR 01 INSPEC reloaded and enhanced  
 NEWS 20 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes  
 NEWS 21 MAR 08 X.25 communication option no longer available after June 2006  
 NEWS 22 MAR 22 EMBASE is now updated on a daily basis

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,  
 CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
 AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.  
 V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT  
<http://download.cas.org/express/v8.0-Discover/>

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\* \* \* \* \* STN Columbus \* \* \* \* \*

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=> file caplus

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	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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 FILE LAST UPDATED: 2 Apr 2006 (20060402/ED)

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=> metabotropic glutamate

5879 METABOTROPIC  
100447 GLUTAMATE  
1102 GLUTAMATES  
100846 GLUTAMATE  
(GLUTAMATE OR GLUTAMATES)  
L1 4363 METABOTROPIC GLUTAMATE  
(METABOTROPIC(W) GLUTAMATE)

=> ?depress?

L2 196569 ?DEPRESS?

=> 11(1)12

L3 543 L1(L)L2

=> metabotropic glutamate receptor

5879 METABOTROPIC  
100447 GLUTAMATE  
1102 GLUTAMATES  
100846 GLUTAMATE  
(GLUTAMATE OR GLUTAMATES)  
643933 RECEPTOR  
590549 RECEPTORS  
766401 RECEPTOR  
(RECEPTOR OR RECEPTORS)  
L4 4123 METABOTROPIC GLUTAMATE RECEPTOR  
(METABOTROPIC(W) GLUTAMATE(W) RECEPTOR)

=> 12(1)14

L5 494 L2(L)L4

=> antidepressant

19799 ANTIDEPRESSANT  
22981 ANTIDEPRESSANTS  
L6 27225 ANTIDEPRESSANT  
(ANTIDEPRESSANT OR ANTIDEPRESSANTS)

=> 13(1)16

L7 73 L3(L)L6

=> d 17 63-73 ti

L7 ANSWER 63 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Physiological antagonism between 5-hydroxytryptamine<sub>2A</sub> and group II  
metabotropic glutamate receptors in prefrontal cortex

L7 ANSWER 64 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI An **antidepressant**-induced decrease in the responsiveness of  
hippocampal neurons to group I **metabotropic glutamate**  
receptor activation

L7 ANSWER 65 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Potential anti-anxiety, anti-addictive effects of LY 354740, a selective  
group II glutamate metabotropic receptors agonist in animal models

L7 ANSWER 66 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Preparation of fluorine-containing amino acid derivatives as group-2



metabotropic glutamate receptor agonists

- L7 ANSWER 67 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Extracts and constituents of Hypericum perforatum inhibit the binding of various ligands to recombinant receptors expressed with the Semliki Forest virus system
- L7 ANSWER 68 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Preparation of 5H-thiazolo[3,2-a]pyrimidines as metabotropic glutamate receptor antagonists and/or agonists.
- L7 ANSWER 69 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI The electrophysiology of prefrontal serotonin systems: therapeutic implications for mood and psychosis
- L7 ANSWER 70 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Differential effects of electroconvulsive shock on the glutamate receptor mRNAs for NR2A, NR2B and mGluR5b
- L7 ANSWER 71 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Antidepressant treatment influences group I of glutamate metabotropic receptors in slices from hippocampal CA1 region
- L7 ANSWER 72 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Influence of imipramine treatment on the group I of metabotropic glutamate receptors in CA1 region of hippocampus
- L7 ANSWER 73 OF 73 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Antidepressant treatment influences cyclic AMP accumulation induced by excitatory amino acids in rat brain

=>

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SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

32.00

32.21

SESSION WILL BE HELD FOR 60 MINUTES

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x

Welcome to STN International! Enter x:

LOGINID:SSSPTA1623PAZ

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 3 DEC 21 IPC search and display fields enhanced in CA/CAPLUS with the  
IPC reform  
NEWS 4 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/